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Christine Kotran
Christine Kotran

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MARKED-UP SUBSTITUTE SPECIFICATION

INHALER FOR BASIC PHARMACEUTICAL AGENTS AND METHOD FOR THE PRODUCTION THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[00001] This application is a National Stage application of International Application No. PCT/EP2004/012947, filed on November 16, 2004, which claims priority of German application number 103 56 925.1, filed on December 5, 2003.

BACKGROUND OF THE INVENTION

Field of the Invention

[00002] The invention relates to devices for administering basic active agents, in particular nicotine, to the human or animal body by ~~means of~~ inhalation. The invention further relates to methods ~~of production by means of which~~ for producing such devices ~~can be obtained~~, as well as [[to]] the use of [[said]] such devices for smoking cessation or for smokeless satisfaction of the craving for nicotine in cases of situational necessity.

Description of the Prior Art

[00003] Nicotine inhalers for administration of nicotine via the air inhaled during inspiration have been known for several years (e.g. US 4 917 120 and US 5 167 242). For some years nicotine inhalers have also been available on the market as smoking cessation products in several European countries ("~~Nicorette~~ NICORETTE®"; Pharmacia/Pfizer). The latter nicotine inhaler is, however, not widely used since with this device only small amounts of nicotine become effective when inhaling. This is due, in particular, to fundamental deficiencies of the known inhaler technologies and the tolerance that can be achieved with these technologies. In particular, the locally irritating effects on the mucous membranes of the respiratory passages, caused by the alkaline properties of nicotine, are ~~of disadvantage~~ disadvantageous since they cause an urge to cough, which results in a decreased absorption of the nicotine vapours released by the inhaler. In this way only very small amounts of nicotine are absorbed by the body.

SUMMARY OF THE INVENTION

[00004] It was therefore the object of the invention to provide a nicotine inhaler which enables absorption of nicotine via the respiratory passages [[that]] and causes as little irritation and is as intense as possible.

[00005] This object is achieved with the devices according to the present invention ~~main claim and the claims dependent thereon~~, as well as with the method of production according to ~~claim 19 and the claims dependent thereon~~ the present invention.

[00006] Accordingly, a device according to the invention ~~is characterized in that~~ ~~it~~ comprises a first preparation which contains a nicotine base or/and another volatile, inhalable basic active agent[[,]]. ~~and that it furthermore~~ The device according to the invention further comprises a second preparation or a plurality of further preparations, which contain ~~said second preparation or at least one of said further preparations containing~~ at least one acid which is volatile and suitable for inhalation. Accordingly, the devices according to the invention are characterized in that upon inhaling, apart from the active agent base (e.g. nicotine base), one or more volatile acid compounds are also inhaled at the same time.

[00007] The devices according to the invention are suitable for the administration of basic agents, in particular nicotine, to the human or animal body by ~~means of~~ inhalation. Suitable basic agents are, for example, selegiline or/and mecamylamine. The combination of nicotine and mecamylamine is used with particular preference for smoking cessation.

[00008] ~~On account of~~ Due to the simultaneous presence of the first preparation, containing a nicotine base (or another active agent base), and of a further preparation, containing a volatile acid, the nicotine base and the volatile acid are volatilised during inhalation, whereby the mixing of the basic and acid vapours leads to the formation of the corresponding nicotine salt (or of the corresponding salt of the other active agent base) in the device. This salt enters the respiratory passages, in the form of liquid drops or in particulate form, along with the inhaled air. Because of the neutral reaction of the mucous membrane to the salt, this type of inhalation shows a considerably better tolerance than can be achieved with known inhalation devices.

[00009] In this connection, it is preferred that said first, nicotine base-containing preparation and said second, acid-containing preparation are applied at separate locations within the device. This way, it is possible to configure the air inlet channels such that, upon inhaling, a part of the air stream flows over the first preparation and

another part of the air stream flows over the second preparation, and that subsequently the two air streams (with the volatilised nicotine base and acid contained therein) combine and can thereafter be inhaled.

[000010] During inhalation, the active agent base (e.g. nicotine base) contained in the first preparation and the volatile acid contained in the second preparation are passively volatilised. This process may optionally be accelerated by application of heat; means suitable for this purpose are known to those skilled in the art.

[000011] When the device according to the present invention is being used, an aerosol is formed in the ambient air flowing in – especially if there are high concentrations of the active agent base and of the acid in the vapours. This aerosol formation is due to the lower volatility of the nicotine salt, the salt mixture or the salt solution drop being formed. The aerosol formation is at the same time the reason for a substantially increased tolerance since nicotine is no longer present in free form and can no longer act as an alkali via the external gas phase. As a result, only the particulate deposition of aerosol particles in the alveoli can lead to the application of active agent in the lung and to absorption (resorption). These aerosol droplets, either as salt components partially dissolved in water or as a solid dispersion, exhibit a far better tolerance ~~on account of~~ due to the neutral (instead of alkaline) mucous membrane reaction than is possible with devices known in the state of the art.

[000012] Aerosol formation is helpful, but it is not imperative for achieving the therapeutic result according to the invention. On the whole, a high dilution of the supplied vapours – thus suppressing the formation of an aerosol – can even be useful in terms of tolerance.

[000013] The size of the aerosol particles formed by the inhalation system according to the invention is, above all, dependent on the velocity of the air flow (flow rate) and on the concentrations of the individual gaseous components (basic active agent and acid, respectively) in the mixing zone.

[000014] Advantageous for alveolar absorption are aerosol particles of a size below 10 µm (mean diameter), in particular 5 to 10 µm.

[000015] According to a preferred embodiment, the inhalation device comprises a first air inlet aperture, a second air inlet aperture and an air outlet aperture. These

apertures are arranged such that the air stream flowing in through the first inlet opening predominantly passes over said first preparation and that the air stream flowing in through the second inlet opening predominantly flows over said second or further preparation(s), the two air streams combining later in their path and exiting the device through said outlet aperture.

[000016] It is furthermore preferred for the device to have oblong recesses, grooves or channels inside, whereby a first and a second air supply channel and an air escape channel are formed. These air flow paths each open towards the outside via said air inlet and air outlet openings, respectively. Said first preparation is located in the oblong recess forming the first air supply channel, and said second preparation is located in the oblong recess forming the second air supply channel. It is preferred for each preparation to be applied in the vicinity of the respective air inlet opening.

[000017] Generally, an approximately equimolar ratio of the molar evaporation rates of the two components (active substance base, acid) is aimed at. If – as described – the nicotine-containing preparation and the acid-containing preparation are applied in two separate air supply channels, which are provided with associated air inlet openings, the respective release rates can be controlled, inter alia, by means of the flow conditions in the two channels. For example, a release rate of 100 µg/10 [[s]] seconds may be provided for an air stream flowing through the first opening and thereby the first air supply channel; in that case – and if acetic acid is used as an acid component – a release rate of approx. 50 mg/10 [[s]] seconds would be suitable for said second air stream.

[000018] With respect to the obtainable release rates, it is preferred that, during one inspiration process, which lasts 1 to 10 [[s]] seconds and during which an inspiration speed of [[0,1]] 0.1 to 1 l/min is reached, an inhalation device according to the present invention releases 5 to 250 µg, preferably 10 to 100 µg, of nicotine base or of another basic agent from said preparation into the inspired air. For example, during one breath lasting 10 [[s]] seconds and at inspiration velocities between 0.1 and 1 l/min, it is possible to administer 100 µg of nicotine base[[;]]. [[this]] This release rate is appropriate for therapeutic purposes.

[000019] To impair the process of inspiration as little as possible, it is preferred for the device to have large passage cross-sections throughout its configuration. This

applies, in particular, to cases where the conduit cross-sections of the air inlet apertures and of the air outlet aperture are dimensioned such that the negative differential pressure in the oral cavity during the process of inspiration does not exceed 300 Pa.

[000020] As the volatile acid, acetic acid is used with preference; other acids may be used as well, provided that they are volatile at room temperature (approx. 15-25 °C) or can be converted to the vapour phase by impact of heat (up to approx. 100 °C) (e.g. lactic acid, malic acid, propionic acid). Even combinations of different acids can be used. Acetic acid, on account of its high volatility, is used at a lower concentration and in a larger total quantity, as well as in combination with additives. Volatile, inhalable basic active agents are understood to be, in particular, those agents which are volatile or which can be converted to the vapour phase at the above-mentioned temperatures.

[000021] Furthermore, according to a specific embodiment, it is provided that the active agent-containing preparation additionally contains at least one solvent suitable for inhalation (preferably ethanol) or/and at least one volatile auxiliary substance (preferably menthol). The acid-containing preparation may likewise contain at least one such solvent or/and at least one volatile auxiliary substance. Suitable volatile auxiliaries are, in particular, flavourings and perfuming substances that are felt to be pleasant (e.g. limonene, eucalyptol, mint oil, camphor or other substances from the terpene group; including combinations of the afore-mentioned substances).

[000022] The invention further encompasses methods for the production of the above-mentioned devices. These methods generally comprise the following steps:

- producing a formed part by deep-drawing or other methods of forming (e.g. injection moulding) known to those skilled in the art, said formed part comprising a first oblong, concave recess for receiving said first preparation, and a second oblong, concave recess for receiving said second preparation;
- introducing a predetermined amount of a first preparation, containing a nicotine base or another basic active agent, into the said first recess;
- introducing a predetermined amount of a second preparation, containing acid(s), into the said second recess.

[000023] The devices according to the invention can be produced in a simple manner and at low cost by using formed parts produced by deep-drawing. A preferred

material suitable for this purpose is a polyester material provided with a coating that is impermeable to the basic agent, especially to nicotine. Suitable for this purpose is, above all, a copolymer of acrylonitrile and methacrylate (Barex®; BP). A polyethylene terephthalate-Barex laminate sheet is used with preference.

[000024] By ~~means of~~ deep-drawing, oblong recesses are provided in a formed part which are to form the two air supply paths. Furthermore, a further oblong recess may be provided which is connected with [[said]] the two recesses and is to form the air outlet channel. The air supply channels and the air outlet channel are of an essentially cylindrical configuration, but they may also be of a geometry that differs therefrom.

[000025] The formed part provided with the recesses forms the bottom part of the device; the upper part may be formed by a second formed part having correspondingly provided recesses, or by a plane film or layer serving as a cover. The upper part and the bottom part are connected with each other in a known manner (e.g. adhesive bonding, sealing), after application of the preparations.

[000026] The recesses forming the air supply channels in the formed part or formed parts may be configured, by providing additional bulges (which may likewise be produced by deep-drawing), such that the vaporisation rate of the respective volatile component can be geometrically limited. This measure results in an additional possibility of accomplishing the preferred delivery of active agent base and acid in equimolar quantities.

[000027] The device is at least partially, but preferably entirely, produced from a material which is impermeable to the active agent(s), particularly from a polyester material which is provided with the above-mentioned coating, and/or from metal foil(s), or combinations of these materials.

[000028] Suitable as base materials for the production of said preparations are, in principle, any materials that may be used for making a reservoir which receives nicotine base or another active agent base or the mentioned volatile acid and which, under the conditions of inhalation, releases these substances by vaporisation to the ambient air. Materials suitable for this purpose are known to those skilled in the art.

[000029] Suitable materials are, for example, polymer materials, as used, for example, in the production of active substance reservoirs of transdermal therapeutic

systems. In this process the active substance (or the acid(s)) is dissolved or dispersed in a polymeric base material (e.g. polyacrylates), optionally with addition of auxiliary substances, and the resultant mass is coated on an inert support and is allowed to dry. Pieces of a certain surface area and layer thickness, with a known content of active agent or acid, are separated from the dried active agent-containing layer. As described, these pieces can then be inserted as the above-mentioned preparations in a device according to the invention. The suitable layer thickness and surface area of the sheet-like preparations introduced into the air flow space of the device are derived from pharmaceutical practice.

[000030] The nicotine preparation inserted in a device according to the invention typically has a content of 10%-wt., and the dose is typically 500 mg. The concentration and dose used in each individual case may deviate from these example values; in particular, the active substance content may be 1 to 80%-wt. and the dose 10 to 1000 mg.

[000031] Suitable as polymer base materials are, in particular, polymers from the group comprising polyethylenes, polypropylenes, silicone polymers (polydimethylsiloxanes) and poly(meth)acrylates.

[000032] The above-mentioned preparations may furthermore be produced by using thermoplastic polymers, the latter being thermally liquefied and the ingredients (basic active agent and/or acid) being metered to the hot polymers. The still liquid preparation is directly applied to the location intended for this purpose of the deep-drawn inhalation device and is allowed to solidify.

[000033] According to a further variant, of the invention a mixture of silicone polymers (polydimethyl siloxane) and crosslinking agent (e.g. a platinum-containing crosslinking agent) is used as the base material. Nicotine base or the volatile acid component is metered in liquid form to this mixture in cold condition. A predetermined amount of this mixture is applied to the respective locations intended for this purpose. After closing the device, it is post-treated under application of heat, whereby a three-dimensional structure of the active agent release preparations is produced.

[000034] The active agent-containing or acid-containing preparation is preferably applied in the vicinity of the air inlet opening of the respective air supply channel.

[000035] The material employed to close the device is preferably a material which is impermeable to the volatile ingredients, as described above.

[000036] In a further preferred embodiment, the inhalation device is covered, after production thereof, with a peelable protective layer impermeable to the basic agent(s). This protective layer will be removed only shortly before use, by the user himself. By means of the protective layer which has been applied a compartment containing the basic active substance(s), and a compartment containing the acid(s) are formed, both compartments being separated from one another in a substantially gas-tight manner and being sealed from the ambient air. In this manner, premature reaction and ageing of the ingredients is prevented. Only after the protective layer has been removed can an exchange of gas [[can]] again take place between the two compartments.

[000037] If necessary, the air inlet and air outlet apertures are also covered with a protective film.

[000038] The devices can advantageously be used for smoker cessation or also for smokeless satisfaction of the craving for nicotine in cases of situational necessity.

[000039] The invention will be illustrated, by way of example and in schematic representation, by ~~means of~~ the appended drawings. The meaning of the reference numerals is identical in all of the drawings unless otherwise indicated.

BRIEF DESCRIPTION OF THE DRAWINGS

[000040] Figure 1A is a longitudinal section view of the device according to the present invention.

[000041] Figure 1B is a longitudinal section view of the device according to the present invention, in an operative condition.

[000042] Figure 1C is a cross-sectional view of the present invention shown through plane X of Figure 1B.

[000043] Figure 2A is a longitudinal section view of an alternative embodiment of the present invention.

[000044] Figure 2B is a cross-sectional view of the present invention shown through plane X of Figure 2A.

[000045] Figure 2C is a longitudinal section view of the alternative embodiment of the present invention shown in Figures 2A and 2B.

[000046] Figure 2D is a cross-sectional view of the present invention shown through plane X of Figure 2C.

[000047] Figure 2E is a cross-sectional view of the present invention shown through plane Y of Figure 2C.

[000048] Figures 3A and 3B are perspective views of another alternative embodiment of the present invention.

[000049] Figure 3C is a plan view of the present invention as shown in Figures 3A and 3B.

[000050] Figure 4A is a perspective sectional view of yet another alternative embodiment of the present invention.

[000051] Figure 4B is a plan view of the present invention as shown in Figure 4A.

[000052] Figure 5 is a cross-sectional view of a modified version of the embodiment of the present invention shown in Figure 4A.

[000053] Figure 6 is a schematic representation of still yet another alternative embodiment of the present invention.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[000054] Fig. 1A shows a device (1) according to the invention in its commercial form (sectional representation). ~~The device~~ Device 1 is formed by an outer wall (2)[[; it]] and has two air flow channels (a, b) which, approximately in the middle thereof, expand to form a respective one of the chambers (3a, 3b) and thereafter combine to form an air escape channel (7).

[000055] In the chambers (3a, 3b) there is a nicotine-containing preparation (5) and an acid-containing preparation (4), respectively.

[000056] Fig. 1A shows the condition of the device prior to use. The inlet and outlet orifices of the air flow channels (a, b) are still closed, and the chambers (3a, 3b) are separated from each other by membranes (13) so that mixing of the two components (4, 5) cannot yet take place.

[000057] Fig. 1B shows (likewise in longitudinal section) the device shown in Fig. 1A in the operative condition after opening of the membranes (13) (e.g. by action of heat or by pushing through) and of the inlet and outlet apertures (A, B, C). The inlet and outlet apertures may be opened, for example, by breaking open or tearing open along a

perforation (11, 12 in Fig. 1A) provided in the device (layer (8) is not shown in Fig. 1B).

[000058] Upon inspiring, air flows through the air inlet aperture (A) and through the air supply channel (a), on the one hand, and through the inlet opening (B) and the air supply channel (b), on the other hand. The dashed arrows indicate the flow direction of the air during inhalation. The two air supply channels (a, b) combine to form the air escape channel (7), having the air outlet aperture (C). In the area of the air supply channel (a) there is a nicotine-containing preparation (5) directly behind the inlet aperture (A), and in the area of the air supply channel (b) there is an acid-containing preparation (4) directly behind the inlet opening (B). When air flows through, nicotine is volatilised from the preparation (5) in the air channel (a), and the acidic compound contained in the preparation (4) is evaporated in air channel (b). In the area of the air escape channel (7), the alkaline and the acidic vapours mix, and an approximately neutral to slightly acidic condition is achieved. The aerosol which has been formed, consisting of ambient air and the nicotine salt contained therein, is inhaled through the outlet opening (C), preferably via the oral cavity.

[000059] Fig. 1C shows a cross-section in plane X of the inhalation device schematically represented in Fig. 1B. The air inlet channels (a, b) are preformed by deep-drawing so that they have a concave shape. In the area of the air channels (a, b) there is the active agent-containing preparation (5) and the acid-containing preparation (4), respectively. The device is covered at the underside by a flat, nicotine-impermeable layer (8).

[000060] Fig. 2A shows (in longitudinal section) a further embodiment of an inhalation device according to the invention in its commercial form. Inlet and outlet apertures (A, B, C) are still closed. The middle region of the channels (a, b) expands to form a respective chamber (3a, 3b). The chambers (3a, 3b) of the individual preparations (4, 5) are arranged side by side and spatially separated from one another, so that mixing of the preparations is not yet possible (condition prior to use).

[000061] Fig. 2B shows a cross-section in plane X of the inhalation device represented in Fig. 2A. The air inlet channels (a, b) and chambers (3a, 3b) are preformed by deep-drawing in the outer wall (2) and are of a concave shape. Inside the

chambers (3a, 3b) there is the active substance-containing preparation (5) and the acid-containing preparation (4), respectively. The device is covered at the underside by a flat, nicotine-impermeable layer (8).

[000062] Fig. 2C is a further longitudinal section of the embodiment shown in Figs. 2A and 2B. The device is shown in its ready-for-use condition. To use the device depicted in Fig. 2A, it is folded, prior to use, along line (14), which may be provided, for example, in the form of a perforation or weakened line, so that by folding along the middle the two air flow channels (a, b) and chambers (3a, 3b) are positioned on top of one another in the longitudinal direction. The apertures of the air inlet and air outlet channels, respectively, may be opened, for example, by breaking open along a perforation (11, 12) provided for that purpose. In this manner a functional inhalation device is obtained. The dashed arrows indicate the direction of air flow during inhalation. A tube or mouthpiece (9) can be slipped on the two outlet apertures (C, C'), thereby forming a joint air outlet channel (7') and a joint outlet aperture (D).

[000063] Fig. 2D shows a cross-section in plane X of the operative device shown in Fig. 2C. The chambers (3a, 3b), formed by the deep-drawn walls (2, 2') and layers (8, 8'), are positioned on top of each other.

[000064] Fig. 2E shows a cross-section in plane Y of the operative device shown in Fig. 2C. The dashed arrows indicate the direction of air flow during inhalation. During inspiration, the air streams (A, B) flow through separated channels (a, b), passing over the preparations (4, 5) located in the chambers (3a, 3b). The resultant vapours or aerosols combine in the region of the air outlet channel (7'), formed by the tube or mouthpiece (9), and leave the device via the outlet aperture (D).

[000065] Figs. 3A and 3B show (in perspective representation) a further embodiment of the device according to the invention, wherein Fig. 3B depicts a tube or mouthpiece (30) into which the cylindrical insert (31) can be inserted. The internal space of the insert (31) is divided, by ~~means of~~ a partitioning wall (32) extending in the longitudinal direction, into two chambers (33, 34) which serve to receive the active agent preparation and the acid component, respectively (not shown). The insert is surrounded by the cylinder barrel (35) (in Fig. 3A it is depicted partially cut open). In the region of the rear end, an aperture (36) is provided in the barrel; said aperture serves

as an air inlet aperture. A further air inlet aperture (37) is provided in the end face (38), which closes the rear end of the insert (31). Figure 3C shows this end face in plan view. The number and arrangement of the apertures may vary.

[000066] During production, a nicotine-containing preparation is placed in the chamber (33, 34), e.g. a carrier material impregnated with nicotine (e.g. a sponge or filter paper), and a carrier material impregnated with a volatile acid (preferably acetic acid) is placed in the respective other chamber; optionally, a flavouring agent or perfuming agent may also be incorporated therewith. All openings, i.e. the front end (V) and the apertures (36, 37) are closed with a suitable protective film or foil.

[000067] Prior to use, the protective films are removed and the insert (31) is inserted into the mouthpiece (30). By sucking on the mouthpiece, air is sucked in via the two rear apertures (36, 37). This air flows through the two chambers (33, 34) over the carrier materials and in doing so takes along the nicotine vapours, acid vapours and, optionally, perfuming agent vapours. These vapours are whirled in the region of the mouthpiece before they enter the oral cavity. The mixing of nicotine and acid vapours facilitates inhalation of nicotine. To this end, it is advantageous for the mouthpiece (30) to be provided with a plurality of protrusions or teeth (39). These are preferably arranged in several offset rows, one after another. The mouthpiece (30) is a substantially cylindrical sleeve open at both ends. It is preferably shorter than the insert (31).

[000068] The protrusions or teeth (39) may also be configured as helical, S-shaped or spiral baffles, thereby achieving better whirling of the air and thus better mixing of the gases.

[000069] Fig. 4A shows a perspective sectional view of a further embodiment of the device according to the invention. This device comprises a sleeve-shaped mouthpiece (30), to which a tube (41) can be rotatably attached or on which a tube (41) can be rotatably slipped or into which a tube (41) can be rotatably inserted (direction of the arrows). Preferably, the end of the mouthpiece (40) is configured such that the tube (41) snaps in when it is slipped onto the mouthpiece. The aperture of the mouthpiece which faces the mouth is, as described in Fig. 3, provided with a plurality of protrusions (39). The internal space of the mouthpiece (40) is divided into four chambers by two partitioning walls. The mouthpiece is open at both ends. That opening which will be

connected with the tube (41) is partially closed. Preferably, at least one sector of the substantially circular cross-section of the mouthpiece is closed, for example two opposite sectors, as shown in Fig. 4B.

[000070] The slip-on tube (41) is open at both ends and inwardly partitioned into four chambers in the same manner (by ~~means of~~ walls (44, 45)) as the mouthpiece. The nicotine-containing preparation and the acid-containing preparation, respectively, are located in two opposite chambers.

[000071] Also provided are embodiments where the mouthpiece and the tube are partitioned into two or three, or more than 4, internal spaces.

[000072] The walls or baffles (44, 45) may also be configured in a helical shape, S-shape or spiral shape, thereby achieving a more intense whirling of the air and consequently a better mixing of the gases.

[000073] The nicotine-containing tube is produced by inserting the nicotine-containing carrier material in a first chamber of the tube, and inserting the acid-containing carrier material into the corresponding, opposite chamber (optionally modified with a perfuming agent). All openings are then closed with a suitable film or foil. In addition, it is possible to fill the remaining chambers of the tube with further active agents or perfuming agents.

[000074] For use, the protective films are removed and the tube (41) is slipped onto the mouthpiece (40), whereby it snaps in. The tube is rotatably engaged, so that by turning the tube (see double arrow) relative to the mouthpiece the filled chambers can be opened and closed. This affords the possibility for the consumer to regulate the air stream he wishes to inhale. If necessary, the open ends of the mouthpiece, respectively of the tube, can be closed with detachable caps.

[000075] Fig. 5 shows (in cross-section) a modification of the embodiment depicted in Fig. 4. The internal space of the mouthpiece (40) and of the tube (41) is divided into four tubular chambers (51, 52, 53, 54); (50) designates the cylindrical wall of the mouthpiece and the tube, respectively.

[000076] In this context, it is ~~of advantage~~ advantageous that the carrier materials impregnated with active agent or acid may be inserted into the tube in the form of "cartridges". In that case, the tube may form a unit with the mouthpiece and be

permanently (but rotatably) connected therewith, which means that the entire device is reusable. The "cartridges" can be stored separately and may be produced so as to have different nicotine contents (or so as to contain different active agents).

[000077] Fig. 6 shows, in schematic representation, a further advantageous embodiment of the device according to the invention. The active agent-containing preparation (not shown) is located in the first compartment (61), which forms a larger gas space wherein the active agent vapours can accumulate. The acid-containing preparation, possibly combined with perfuming agents, is located in a second compartment (62). The broad arrows indicate the direction of the air streams occurring while inhaling. Air is sucked in through the inlet apertures (64, 65). These may be provided with valves in order to prevent premature mixing of the ingredients (active agent, acid) or/and prevent them from escaping to the outside.

[000078] Upon inhaling through the mouthpiece (63), the air flows into the device along two different paths: (i) Air flows through lateral apertures (64) into the compartment (61) and in the process flushes the gas space, which is presaturated with vapour pressure, into the mixing zone in front of the mouthpiece (63)[[.]]; and (ii) ~~Simultaneously~~ simultaneously, air is sucked in through the lateral apertures (65) into the second compartment (62). In the process, this air also flushes the auxiliary substances (acid, possibly flavouring agents) into the mixing zone in front of the mouthpiece (63). In the mixing zone, the two air flows mix with each other. During this mixing process, the desired neutralisation of the active agent base takes place.

[000079] What has been described above are preferred aspects of the present invention. It is of course not possible to describe every conceivable combination of components or methodologies for purposes of describing the present invention, but one of ordinary skill in the art will recognize that many further combinations and permutations of the present invention are possible. Accordingly, the present invention is intended to embrace all such alterations, combinations, modifications, and variations that fall within the spirit and scope of the appended claims.